

Eukaryon

Volume 6 *Evolving Connections*

Article 14

3-1-2010

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Chemical Wonders of Biological Processes Link Humans, Bacteria and Fireflies

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Sanitizing products and modern-day drugs contain antibiotic compounds to which microorganisms are becoming increasingly resistant.

As little kids, most of us froze in amazement as the fireflies we captured in our jar brightened up our backyards with their neon glow. Within our childlike brains, billions of neurons communicate with each other through neural connections to perceive the glow. Captivated, our hearts raced with excitement at the wonders of these bugs. Behind all of these biological events is the chemical nitric oxide. Nitric oxide is responsible for the luminescent glow of the fireflies, the communication between neurons as a neurotransmitter, and the beating of our hearts. Science is showing us that nitric oxide has roles in many other biological processes as well. Like humans, some bacteria also contain nitric oxide. Bacteria with the enzymes, appropriately called bacterial nitric oxide synthases (bNOS), are capable of producing nitric oxide. However, the role of these enzymes has remained largely obscure. Recently, scientists have determined that the nitric oxide produced by these bacteria functions in increasing their resistance against a wide spectrum of antibiotics. Furthermore, these bacteria are

capable of surviving in environments rich with antibiotic-producing microorganisms.

At New York University's School of Medicine, scientists have recently discovered that the gene known as *nos* codes for the bNOS enzyme that produces nitric oxide in bacteria. Therefore, its presence in the genome of certain bacteria will suggest better resistance of antimicrobials. In this recently published study by Ivan Gusarov et al., three populations of bacteria with a knockout or wildtype *nos* gene were tested with different antimicrobials to determine the extent of the role that *nos* played on bacterial resistance to these substances. A wildtype bacterial culture was capable of surviving exposure to antimicrobials, yet knockout *nos* experienced significant sensitivity to the antibiotics.

Additionally, a different gene present in some bacteria known as *Sod A* is believed to be capable of countering the effects of reactive oxygen species. Reactive oxygen species, also known as free radicals, are byproducts of cellular metabolism capable of damaging many cellular structures because they oxidize molecules in the cell. To determine whether *Sod A* influences antimicrobial resistance, Gusarov knocked out *Sod A* in both a knockout *nos* strain and a wildtype strain of bacteria. When these strains were exposed to antimicrobials, they noticed that the strain with both knockouts experienced even greater sensitivity, demonstrating that *Sod A* has a role in increasing the resistance of bacteria against antimicrobials in conjunction with *nos*.

These new findings give scientists possible ways of effectively using antimicrobials. With the understanding that nitric oxide synthases in bacteria give the bacteria greater resistance to antimicrobials, scientists can now find ways to inhibit this enzyme and thus create an effective way of reducing bacterial resistance. Some antimicrobials affect bacteria by raising the amount of reactive oxidative species; *Sod A* counters these effects to a certain extent. Thus, targeting *Sod A* in these species, as well as bNOS, will lead to more efficient reduction of growth.

From aiding in the survival of microscopic organisms to the survival of insects and even humans, nitric oxide's role in the ecosystem spans the array of many biological systems. For scientists interested in this chemical, the discovery of the functions of nitric oxide in many biological systems brings about as equal excitement as that which they probably experienced when they chased the neon glow of the firefly when they were young.

Full Citation: Gusarov, I., K. Shatalin, M. Starodubtseva, & E. Nudler. (2009). Endogenous nitric oxide protects bacteria against a wide spectrum of antibiotics. *Science*, 325(5946), 1380-1384.

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